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Introduction

Rudolf Zubler

Division of Hematology, Geneva University Hospital, Geneva, Switzerland

The contributions to this issue of Springer Seminars in Immunopathology provide important updates on key functions of antibodies in normal defenses, autoimmunity, and immunoregulation/therapeutic immunomodulation, as well as on the regulation of the B lymphocyte responses that produce them, and the mechanisms underlying their diversity.

Antibodies serve as B cell receptors (BCR) for antigens in immune responses. Early forms of the BCR, expressed in pro-B and pre-B cells, regulate B cell maturation. Evidence indicating that ligand-independent signaling occurs in immature B cell stages, and also for the maintenance of viability of mature B cells, is reviewed by Ezequiel Fuentes-Pananá and John Monroe.

The conflict between the generation of antibody diversity and the maintenance of self-tolerance was recognized by the early immunologists. Current knowledge of mechanisms of tolerance that operate at different stages of lymphocyte maturation in central and peripheral immune organs, and particularly the problem of tolerance to the central nervous system, is reviewed by Antonio Iglesias.

Somatic hypermutation of variable-region genes (V, D, J) is a B-cell-specific feature of adaptive immunity. Which human B cell subsets express hypermutated antibodies, the mutation patterns and the mechanisms – the emergent roles of multiple error-prone DNA polymerases – involved in this aspect of antigen receptor/antibody repertoire diversity are reviewed by Nancy Longo and Peter Lipsky.

Repertoires of antibodies reacting with polysaccharide-encapsulated bacteria have been extensively investigated (V-genes, mutations). These organisms are medically important; their key antigens are of the T-independent type 2 (T12) and young children are particularly susceptible. Conjugate vaccines for the stimulation of T-dependent responses to T12 are among the most remarkable achievements of immunology, as reviewed by Elisabeth Adderson.

Different subsets of newly generated B cells home to microenvironments optimal for either T-dependent or T-independent responses. Functionally experienced, V(D)J

Correspondence to: R. Zubler, Division of Hematology, Geneva University Hospital, 1211 Geneva 14, Switzerland

mutated memory B cells produced in T-dependent responses then also become available for T-independent responses. Many memory B cells conserve their class-switch capacity, others are isotype-stabilized, as reviewed by Rudolf Zubler.

Antibodies have the capacity to regulate their own production, and antibody feedback-suppression of B cell responses is powerful. This function, as well as antibody-mediated enhancement, involves a variety of mechanisms that are isotype-dependent and/or epitope-specific. All immunoglobulin isotypes have immunoregulatory effects, as reviewed by Birgitta Heyman.

Effector functions of antibodies are also largely isotype-specific, but the role of different Fc receptors or complement in the immunopathogenicity of antibodies in vivo is often not predictable from studies in vitro. The combined effects of isotype and valency/affinity for the antigen can be analyzed quantitatively in appropriate in vivo models, as reviewed by Shozo Izui et al.

In accordance with their diverse biological functions, mixtures of human antibodies have strong immunomodulatory effects in certain autoimmune diseases. Clinical experience with high-dose i.v. immunoglobulins in various diseases, deriving from controlled or still preliminary studies, is critically reviewed by Lubica Rauova, Jozef Rovensky and Yehuda Schoenfeld.